Enteric-Coated Mycophenolate Sodium is Therapeutically Equivalent to Mycophenolate Mofetil in \textit{de novo} Renal Transplant Patients

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The introduction of mycophenolate mofetil (MMF) represented a major advance in transplant medicine, although optimal use may be limited by gastrointestinal (GI) side-effects. An enteric-coated formulation of mycophenolate sodium (EC-MPS; myfortic\textsuperscript{®}) has been developed with the aim of improving the upper GI tolerability of mycophenolic acid. Therapeutic equivalence of EC-MPS (720 mg b.i.d.) and MMF (1000 mg MMF b.i.d.), with concomitant cyclosporine microemulsion (Neoral\textsuperscript{®}) and corticosteroids, was assessed in 423 \textit{de novo} kidney transplant patients recruited to a 12-month, double-blind study. Efficacy failure (biopsy-proven acute rejection [BPAR], graft loss, death or loss to follow up) at 6 months (EC-MPS 25.8\% vs. MMF 26.2\%; 95\% CI: [−8.7, +8.0]) demonstrated therapeutic equivalence. At 12 months, the incidence of BPAR, graft loss or death was 26.3\% and 28.1\%, and of BPAR alone was 22.5\% and 24.3\%, for EC-MPS and MMF, respectively. Among those with BPAR, the incidence of severe acute rejection was 2.1\% with EC-MPS and 9.8\% with MMF (p = ns). The safety profile and incidence of GI adverse events were similar for both groups. Within 12 months, 15.0\% of EC-MPS patients and 19.5\% of MMF patients required dose changes for GI adverse events (p = ns). Enteric-coated-MPS 720 mg b.i.d. is therapeutically equivalent to MMF 1000 mg b.i.d. with a comparable safety profile.

Key words: EC-MPS, efficacy, enteric-coated mycophenolate sodium, immunosuppression, MMF, MPA, mycophenolate mofetil, mycophenolic acid, myfortic\textsuperscript{®}, renal transplant

Introduction

Acute rejection in organ transplantation increases the risk of chronic allograft nephropathy and reduces graft survival (1). An important advance in patient transplant care was the introduction of mycophenolate mofetil (MMF), the morpholino ester of mycophenolic acid (MPA). Immunosuppressive therapy with MPA is associated with decreased graft rejection incidence and prolonged graft survival (2–4). Mycophenolic acid is a potent, selective, competitive and reversible inhibitor of inosine monophosphate dehydrogenase (IMPDH) and therefore inhibits the \textit{de novo} pathway of guanosine nucleotide synthesis without incorporation into DNA. T- and B-lymphocyte proliferation is critically dependent upon the \textit{de novo} purine synthesis pathway, whilst other cell types can utilize salvage pathways for purine synthesis. Mycophenolic acid therefore has a more potent cytostatic effect on lymphocytes than on other cells (5,6). Nevertheless, the use of MPA and, in particular, MMF has been associated with gastrointestinal (GI) side-effects (7).

Enteric-coated mycophenolate sodium (EC-MPS; myfortic\textsuperscript{®}, Novartis Pharma AG, Basel, Switzerland) is an enteric-coated formulation delivering MPA. Enterico-coated-MPS has been developed with the aim of improving the upper GI tolerability of MPA. Enteric-coated-MPS 720 mg and MMF 1000 mg contain near equimolar MPA content and provide similar MPA exposure (8). Consistent with the enteric-coated design, delivery of MPA is delayed (8).

The purpose of this study was to demonstrate the therapeutic equivalence of EC-MPS and MMF and to compare their safety profiles.

Methods

This phase III, international, randomized, double-blind, parallel group, 12-month study involving patients undergoing \textit{de novo} renal transplantation was performed at 30 centers in Austria, Canada, Germany, Hungary,
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Italy, Norway, Spain, UK and USA. Written informed consent was obtained from all patients and the study was conducted in full compliance with EEC Directive 91/670, the US 21 Code of Federal Regulations and the amended Declaration of Helsinki.

The study design comprised a screening visit, a baseline period (within 2 h of randomization), and a double-blind treatment period. After screening, patients who fulfilled the inclusion/exclusion criteria were randomized equally into one of two treatment groups: 1000 mg b.i.d. MMF or 720 mg b.i.d. EC-MPS. In total, 213 patients were assigned to the EC-MPS treatment group and 210 to the MMF treatment group. Concomitant immunosuppressive therapy included cyclosporine microemulsion (ME-CsA; Neoral®, Novartis Pharma AG, Basel, Switzerland) and corticosteroids.

Inclusion criteria
Patients of either sex, aged 18–75 years (except for Austria: aged 19–75 years), who were recipients of a first cadaveric, living-unrelated or human leukocyte antigen (HLA)-mismatched living-related donor kidney transplant, and who gave written informed consent, were eligible to participate in the study. Females of childbearing age were required to test negative for pregnancy.

Exclusion criteria
Patients were excluded if their graft originated from a nonheart beating donor, if they had undergone a previous kidney transplant or had previously received any other transplanted organ. Patients who had a positive T-cell crossmatch, ABO incompatibility against the donor, or panel reactive antibodies (PRAs) > 50% before transplantation were also excluded. Additional exclusion criteria included positive HIV, a positive hepatitis B surface antigen, thrombocytopenia (<75 000 cells/mm³), absolute neutrophil count of <1500 cells/mm³, and/or leukocytopenia (<2500 cells/mm³), and/or hemoglobin <6 g/dL, clinically significant infections requiring continued therapy, or the presence of severe diarrhea, active peptic ulcer disease, uncontrolled diabetes mellitus or malignancy (other than local basal or squamous cell carcinoma of the skin) within the last 5 years. The use of any other investigational drug within 4 weeks before screening was prohibited. Female patients of childbearing age who were unwilling to use an effective form of contraception for the duration of the study and for 6 weeks following discontinuation of study medication were excluded.

Efficacy evaluations
Key efficacy analyses were performed on the intent-to-treat (ITT) population, which comprised patients who were randomized and had at least one assessment after the start of trial medication. The primary efficacy evaluation was treatment failure, defined as the incidence of biopsy-proven acute rejection (BPAR), graft loss, death or loss to follow up, within 6 months of the start of treatment. The secondary efficacy endpoints were the incidence of BPAR, graft loss, death, clinically diagnosed rejection, treated rejection, rejection requiring antibody therapy, and biopsy-proven chronic rejection evaluated at 6 and 12 months.

Safety evaluations
The patient population evaluated for safety criteria included all randomized patients who received at least one dose of study medication and had at least one safety/tolerability assessment subsequently. Evaluated safety criteria comprised adverse events (AEs); any newly occurring condition or disability or worsening of a condition observed at baseline, hematology and biochemistry profiles, infections, neoplastic disease, and discontinuation of study drug as a result of an AE.

Statistical analyses
Primary efficacy was assessed by the two-sided 95% confidence intervals (95% CI) of the difference in event rates, which had to be entirely within the predetermined interval [−12, +12] to conclude equivalence. Even though no adjustment was made for multiple comparisons, several other efficacy and safety parameters, including GI AEs, were tested statistically as exploratory analyses. Z-test statistics, Cochran–Mantel–Haenszel test and Kaplan–Meier methodology were used to assess efficacy events. Safety variables, including GI AEs, were evaluated by means of frequency distribution and descriptive statistics. Laboratory variables were tested for baseline comparability using the Wilcoxon rank sum test. Categorical safety variables were tested using the Chi-square or Fisher’s exact tests, and confidence intervals for differences in incidence rates were obtained using exact or asymptotic normal approximation methods. All significance tests were conducted at the 0.05 significance level and were two-sided. Only p-values that reached significance level are reported.

Study size determination, randomization and blinding procedure
The initial sample size, set at 200 patients per group, was based on the following assumptions: the probability of treatment failure, defined as BPAR, graft loss, death or loss to follow up, within 6 months was 20% for both groups; EC-MPS is clinically equivalent to MMF when the 95% CI lies entirely within the predetermined interval [−12, +12], and the power for claiming clinical equivalence is 0.85.

Randomization was undertaken immediately before first administration of study medication (day 1) by using the center’s lowest available randomization number. Patients were randomized according to a computer-generated schedule in order to guarantee that patients were distributed equally between the treatment groups. Study medication was packaged so as to maintain the double-blind trial design and to allow dose reduction. The patients, investigators, study center personnel and any Novartis personnel in direct contact with the study centers were blinded until the 12-month analysis was completed.

Immunosuppression
After randomization, patients received either MMF 1000 mg b.i.d. or EC-MPS 720 mg b.i.d. plus matching placebo within 48 h postreperfusion of the kidney. Patients were instructed to take two enteric-coated tablets and four capsules b.i.d. At the discretion of the investigator, if a patient displayed a leukocyte count <4000 cells/mm³ or a neutrophil count <1500 cells/mm³ or experienced other moderate to severe AEs, the study medication dose could be reduced by 50% or eliminated completely until these events resolved.

ME-CsA treatment was initiated within 24 h of transplant at 10 mg/kg/day and adjusted to maintain a trough level (C0) in the following target ranges: 200–400 ng/mL for days 1–7, 200–300 ng/mL for weeks 1–4, 150–250 ng/mL for months 2–6 and 100–200 ng/mL for months 7–12. Prednisone (or equivalent) dose was tapered according to local practice, but not to less than 5 mg/day for at least 6 months.

Induction therapy with antithymocyte or antilymphocyte antibody preparations, such as ALG, ATG, OKT3, or anti-CD25 monoclonal antibodies, was allowed in centers where all patients routinely receive induction therapy. In such centers, antibody use was to be consistent in all study patients in order to avoid imbalance between treatment groups.

Rejection
Acute rejection episodes were verified by core biopsies before or within 24 h following the start of antirejection therapy and rated according to the Banff 97 classification (9). Methylprednisolone was given at a dose of 500–1000 mg/day i.v. for 3 days. In cases of Grade III/IV vascular rejection or continuing evidence of rejection, administration of ATG or OKT3 antibody preparations was allowed. Steroid-resistant rejections were to be treated with OKT3. Study medication could be interrupted during antirejection therapy.

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**Other concomitant therapies**

Cytomegalovirus (CMV) prophylaxis, at least during the first 3 months of the study, was recommended, except where both donor and recipient tested negative for CMV, and was administered according to local practice. Treatment with acyclovir was to be avoided because it is suspected to interact with the pharmacokinetics of MPA. Pneumocystis carinii prophylaxis was recommended.

**Results**

A total of 423 patients were recruited into the study and randomized to either EC-MPS (n = 213) or MMF (n = 210) treatment groups.

There were no significant differences between the demographic characteristics of the two groups (Table 1). In both groups, the majority of patients were male (64.3% for EC-MPS and 67.6% for MMF) and Caucasian (87.8% for EC-MPS and 89.0% for MMF). Transplants from cadaveric donors were received by a total of 83.7% of patients. In total, 20.7% of EC-MPS patients compared with 13.3% of MMF patients received transplants with cold ischemia times ≥ 24 h (p = 0.051). In addition, 16.9% of EC-MPS patients were donor CMV-positive/recipient CMV-negative compared with 12.4% of MMF patients (p = ns). Frequency of HLA mismatches was similar in both treatment groups and comparable between the treatment groups, regardless of the origin of the donor (cadaveric or living) (Table 1). Delayed graft function, defined as a need for dialysis during the first week post transplant, occurred in a similar proportion of patients in both treatment groups (18% for EC-MPS and 17% for MMF).

A total of 151 patients (70.9%) in the EC-MPS group and 158 patients (75.2%) in the MMF group completed 12 months of study treatment (p = ns). Most treatment discontinuations occurred in the first 6 months. In total, 20.2% of EC-MPS patients and 18.6% of MMF patients discontinued treatment because of AEs, laboratory abnormalities, or death. The major reasons for discontinuation of study drug are summarized in Table 2.

**Efficacy**

Within the first 6 months post-transplant, on the basis of ITT analysis, the incidence of efficacy failure, defined as the incidence of BPAR, graft loss, death or loss to follow up, was similar for EC-MPS and MMF (25.8% and 26.2%, respectively). The 95% CI for efficacy failure was [−8.7, +8.0], indicating clinical equivalence between the two study treatments. At 12 months, the incidence of BPAR, graft loss or death was 26.3% and 28.1% for EC-MPS and MMF, respectively (95% CI: [−6.3, +6.7]) and the incidence of BPAR, graft loss, death or loss to follow up was 28.6% and 28.1% for EC-MPS and MMF, respectively (95% CI: [−8.0, +9.1]) (Figure 1). The incidence of BPAR at 12 months was 22.5% and 24.3% for EC-MPS and MMF, respectively (95% CI: [−9.8, +6.3]). In patients who experienced BPAR, the proportions of mild acute (Grade Ia/Ib) and moderate acute (Grade IIa/IIb) rejection episodes, according to Banff classification, were comparable in both treatment arms.

### Table 1: Patient baseline characteristics of the intent-to-treat population

<table>
<thead>
<tr>
<th></th>
<th>EC-MPS (n = 213)</th>
<th>MMF (n = 210)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years; mean ± SD)</td>
<td>47.1 ± 11.84</td>
<td>47.2 ± 11.55</td>
</tr>
<tr>
<td>Gender (%)</td>
<td></td>
<td></td>
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<tr>
<td>Male</td>
<td>64.3</td>
<td>67.6</td>
</tr>
<tr>
<td>Female</td>
<td>35.7</td>
<td>32.4</td>
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<tr>
<td>Race (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>87.8</td>
<td>89.0</td>
</tr>
<tr>
<td>Black</td>
<td>8.0</td>
<td>6.2</td>
</tr>
<tr>
<td>Oriental</td>
<td>1.4</td>
<td>1.0</td>
</tr>
<tr>
<td>Other</td>
<td>2.8</td>
<td>3.8</td>
</tr>
<tr>
<td>Cadaveric donor (%)</td>
<td>85.0</td>
<td>82.4</td>
</tr>
<tr>
<td>Living donor (%)</td>
<td>15.0</td>
<td>17.6</td>
</tr>
<tr>
<td>HLA mismatch (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–3</td>
<td>62.0</td>
<td>60.0</td>
</tr>
<tr>
<td>4–6</td>
<td>37.1</td>
<td>38.8</td>
</tr>
<tr>
<td>Cadaveric donor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–3</td>
<td>61.3</td>
<td>60.7</td>
</tr>
<tr>
<td>4–6</td>
<td>37.6</td>
<td>39.3</td>
</tr>
<tr>
<td>Living donor</td>
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<td></td>
</tr>
<tr>
<td>0–3</td>
<td>65.6</td>
<td>56.8</td>
</tr>
<tr>
<td>4–6</td>
<td>34.4</td>
<td>43.2</td>
</tr>
<tr>
<td>Donor CMV+ / recipient CMV− (%)</td>
<td>16.9</td>
<td>12.4</td>
</tr>
<tr>
<td>Cold ischemia time (h; mean ± SD)</td>
<td>17.0 ± 9.2</td>
<td>15.6 ± 8.8</td>
</tr>
<tr>
<td>Cold ischemia time ≥24 h (%)</td>
<td>20.7</td>
<td>13.3</td>
</tr>
</tbody>
</table>

*p = 0.051.

### Table 2: Major reasons for discontinuation of study drug during the study

<table>
<thead>
<tr>
<th></th>
<th>EC-MPS (n = 213)</th>
<th>MMF (n = 210)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discontinuation due to adverse events</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>10 (4.7)</td>
<td>11 (5.2)</td>
</tr>
<tr>
<td>Infections</td>
<td>5 (2.3)</td>
<td>7 (3.3)</td>
</tr>
<tr>
<td>Neoplasms</td>
<td>3 (1.4)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>2 (0.9)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Increased blood creatinine</td>
<td>1 (0.5)</td>
<td>3 (1.4)</td>
</tr>
<tr>
<td>Stroke</td>
<td>0 (0)</td>
<td>1 (0.5)</td>
</tr>
<tr>
<td>Polynephropathy</td>
<td>0 (0)</td>
<td>1 (0.5)</td>
</tr>
<tr>
<td>Other reasons for discontinuation</td>
<td>26 (12.2)</td>
<td>23 (11.0%)</td>
</tr>
<tr>
<td>Abnormal laboratory values</td>
<td>1 (0.5)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Unsatisfactory therapeutic effect</td>
<td>11 (5.2)</td>
<td>8 (3.8)</td>
</tr>
<tr>
<td>Protocol violation</td>
<td>5 (2.3)</td>
<td>5 (2.4)</td>
</tr>
<tr>
<td>Withdrawal of consent</td>
<td>2 (0.9)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Death</td>
<td>1 (0.5)</td>
<td>4 (1.9)</td>
</tr>
<tr>
<td>Loss to follow up</td>
<td>1 (0.5)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Graft loss</td>
<td>5 (2.3)</td>
<td>6 (2.9)</td>
</tr>
</tbody>
</table>
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Figure 1: Efficacy of enteric-coated mycophenolate sodium (EC-MPS) and mycophenolate mofetil (MMF) at 12 months (p = ns). *Biopsy-proven acute rejection, graft loss or death to follow up: 28.6% and 28.1% for EC-MPS and MMF, respectively; [95% CI: [−8.0, +9.1]; p = ns].

groups. The incidence of severe acute rejection episodes (Grade III) was 2.1% in the EC-MPS group vs. 9.8% in the MMF group (p = ns).

Biopsy-proven chronic rejection diagnosed between 3 and 12 months was infrequent in both groups (EC-MPS 2.8% and MMF 6.2% at 12 months; p = ns) and the incidence of graft loss or death was similar in both groups (EC-MPS 5.2% and MMF 6.7%; p = ns) (Figure 1).

Safety
The overall incidence and profile of AEs were comparable for both of the treatment groups. The majority of AEs were mild or moderate in severity. The incidence of severe AEs (including infections) was also comparable between treatment groups (Figure 2). The incidence of suspected drug-related AEs was 53.1% in patients receiving EC-MPS and 60.5% in patients receiving MMF, the difference not being statistically significant. The incidence and profile of serious AEs were similar between the treatment groups. Serious infections were recorded in 22.1% of patients receiving EC-MPS and in 27.1% of patients receiving MMF (p = ns) (Figure 2). The incidence of serious pneumonia was statistically significantly lower in patients receiving EC-MPS than in those receiving MMF (0.5% vs. 4.3%; p = 0.01).

A similar proportion of patients experienced a GI AE in both groups over the 12-month study period (EC-MPS 80.8% vs. MMF 80.0%; p = ns). The frequency of upper GI AEs – defined as the occurrence of symptoms affecting the intestine from the esophagus to the duodenum – and nonupper GI AEs – defined as AEs affecting the oral cavity, lower intestine or undetermined location – were also comparable in each group. By month 12, 53.5% of EC-MPS patients and 54.3% of MMF patients had experienced upper GI AEs, whilst nonupper GI AEs were reported in 68.5% and 68.1% of EC-MPS and MMF patients, respectively. The incidence of dose changes – as measured by the composite of discontinuation, dose reduction or dose interruption – for GI AEs was 13.1% with EC-MPS and 17.1% with MMF within 6 months (p = ns) and 15.0% with EC-MPS vs. 19.5% with MMF within 12 months (p = ns) (Figure 3).

Cytomegalovirus infection
Over the 12-month study period, the incidence of CMV infection was similar in each group of patients (21.6% and 20.5% for EC-MPS and MMF, respectively), as was the incidence of CMV disease (EC-MPS 4.7% and MMF 4.3%).

Malignancies
Malignancies or lymphoma were reported in five patients from each treatment group. Lymphoma was reported in two EC-MPS patients (one of which was a cutaneous T-cell lymphoma diagnosed 9 days after treatment commenced),

Figure 2: Frequency and severity of adverse events (AEs), including infections, during the 12-month study period.

Figure 3: Incidence of dose changes as a result of gastrointestinal adverse events (GI AEs) (p = ns). Dose changes include dose reductions, interruptions or discontinuations.
of GI AEs. However, additional studies are needed before
finite conclusions can be drawn regarding the ben-

Concomitant immunosuppressive therapies

Use of antibody therapy as an induction treatment was
equivalent in both treatment groups: 39.4% and 42.9%
of patients in the EC-MPS and MMF groups, respectively
(Table 3). The most common therapies were basiliximab
(22.1% EC-MPS patients; 23.8% MMF patients) and anti-
lymphocyte or antithymocyte antibodies (16.4% EC-MPS
patients; 17.1% MMF patients). In addition, no differences
in concomitant corticosteroid dose, ME-CsA dose, or cy-
closporine blood levels achieved were noted between the
two treatment groups during the 12-month study period
(Table 4).

Discussion

The addition of MMF to the immunosuppressive regimen
used in renal transplantation has led to substantial reduc-
tions in the incidence of kidney graft acute rejection (2,3)
and to an improvement in long-term graft survival as well
as graft function as measured by serum creatinine (4,10).
Enteric-coated-MPS is an enteric-coated formulation
delivering MPA.

In accordance with the design of the study, therapeutic
equivalence of EC-MPS and MMF in de novo renal trans-
plant patients was statistically demonstrated. The 95% CI
for the difference in event rates of the primary efficacy
variable between the two treatment groups at 6 months
was entirely contained within the interval of $[-12, +12]$
therefore establishing equivalence. No statistically signi-
cificant differences were observed in the measured efficacy
parameters throughout the entire study period and inci-
dence rates of BPAR, death, graft loss and loss to follow
up remained similar between the two treatment groups at
12 months. The incidence of BPAR was also similar be-
tween the two treatment groups. The incidence of study
drug discontinuation was similar to that observed in other
blinded studies (2,11).

The overall safety profile and hematologic profile were simi-
lar between the two treatment groups. The incidence of
CMV infection and CMV disease observed during the study
were also similar. The overall incidence of serious infec-
tions was 22.1% in the EC-MPS group and 27.1% in the
MMF group ($p = \text{ns}$) (Figure 2), with the incidence of se-
rious pneumonia being statistically significantly lower in
the EC-MPS group (0.5% vs. 4.3%; $p = 0.01$). No dif-
fERENCE in the overall incidence of GI AEs was observed
between EC-MPS and MMF in the context of this double-
blind, double-dummy, randomized trial, which was not de-
gined to statistically detect differences between treat-
ment groups in terms of GI tolerability. A nonsignificant
trend towards fewer dose reductions or dose discontinua-
tions in response to GI AEs was observed in the EC-MPS
group compared with the MMF group ($p = \text{ns}$), which may
suggest that EC-MPS has a positive effect on the severity
of GI AEs. However, additional studies are needed before
any definitive conclusions can be drawn regarding the ben-
efit of the enteric-coated formulation on GI tolerability.

Enteric-coated-MPS and MMF demonstrated therapeutic
equivalence in de novo renal transplant patients, with
a comparable safety profile. Enteric-coated-MPS offers

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### Table 3: Use of antibody induction treatment during the study

<table>
<thead>
<tr>
<th></th>
<th>EC-MPS (n = 213)</th>
<th>MMF (n = 210)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibody induction (%)</td>
<td>39.4</td>
<td>42.9</td>
</tr>
<tr>
<td>Basiliximab (%)</td>
<td>22.1</td>
<td>23.8</td>
</tr>
<tr>
<td>Anti-lymphocyte/antithymocyte antibodies (%)</td>
<td>16.4</td>
<td>17.1</td>
</tr>
<tr>
<td>Daclizumab (%)</td>
<td>0.9</td>
<td>1.4</td>
</tr>
<tr>
<td>Murumonab CD 3 (%)</td>
<td>0.5</td>
<td>0.5</td>
</tr>
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</table>

### Table 4: Dose of concomitant immunosuppressive therapy during the 12-month study

<table>
<thead>
<tr>
<th></th>
<th>EC-MPS (n = 213)</th>
<th>MMF (n = 210)</th>
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<tbody>
<tr>
<td>Corticosteroids</td>
<td></td>
<td></td>
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<tr>
<td>Mean dose at 6 months (mg/kg/day)</td>
<td>0.1 ± 0.12</td>
<td>0.1 ± 0.09</td>
</tr>
<tr>
<td>Mean dose at 12 months (mg/kg/day)</td>
<td>0.1 ± 0.10</td>
<td>0.1 ± 0.08</td>
</tr>
<tr>
<td>ME-CsA</td>
<td></td>
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</tr>
<tr>
<td>Mean dose at 6 months (mg/kg/day)</td>
<td>3.7 ± 1.47</td>
<td>3.5 ± 1.35</td>
</tr>
<tr>
<td>Mean dose at 12 months (mg/kg/day)</td>
<td>3.5 ± 1.29</td>
<td>3.2 ± 1.25</td>
</tr>
<tr>
<td>Mean trough level at 6 months (ng/mL)</td>
<td>190.1 ± 76.35</td>
<td>196.3 ± 74.34</td>
</tr>
<tr>
<td>Mean trough level at 12 months (ng/mL)</td>
<td>166.3 ± 65.01</td>
<td>170.6 ± 62.51</td>
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</table>

Mean ± SD.
transplant physicians and their patients an alternative MPA therapy that is as effective and safe as MMF.

Acknowledgments

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